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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,945	05/02/2001	Neil P. Desai	420052000127	6174

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/847,945	DESAI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-17 and 31-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-17, 31-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Request for Continued Examination and Amendments/Remarks filed 12/20/06 is acknowledged. Claims **1, 3-17, 31-78** are pending in this application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of claims 1, 3-17, 29, 31-33, 39-41, 47-49, and 55 under 35 U.S.C. 103(a) as being unpatentable over Kunz et al (5,733,925) of Westesen et al (6,197,349) is withdrawn in view of the amendments of 12/20/06.

Claims 1, 3-17, 31-33, 38-41, 46-49, 54-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (5,439, 686) in view of Kinsella et al (5,616,608) in further view of Westesen et al (6,197,349) or vice-versa wherein claims 1, 3-17, 31-33, 38-

41, 46-49, 54-77 are rejected over Kinsella et al in view of Desai et al in view of Westesen et al (6,197,349).

Desai et al teach an anticancer (antineoplastic) drug, specifically paclitaxel (taxol), is suspended in a protein walled shell. See abstract. The shell is not greater than about 10 microns, preferably less than 5 microns, and most preferably less than 1 micron (1000 nanometers). See column 5, lines 30-40. For intravenous administration, the particles may have a diameter size from 0.1-5 microns. See column 9, lines 15-16. A preferred protein for the shell is albumin. See column 6, lines 40-45 and example 4. Taxol exhibits a unique mode of action on microtubule proteins responsible for the formation of the mitotic spindle. See column 1, lines 20-30. Desai teaches administration of the microparticulates are advantageous in targeting specific sites in the body; allows for the administration of water-insoluble actives; reduces administration time. See column 3, lines 60-67 to column 4, lines 1-5. The particles also are stable and low in toxicity. See examples 5 and 7.

Desai does not teach the instant methodology of treating non-cancerous cell proliferation in blood vessels. Further, Desai does not teach an amorphous drug.

Kinsella teaches a method of treating atherosclerosis or restenosis using microtubule stabilizing agent such as taxol or taxol derivatives. It should be noted that restenosis is the excessive proliferation of smooth muscle cells, i.e. non-cancerous cells, in the blood vessel. During angioplasty, intraarterial balloon catheter inflation results in endothelialization, disruption of the internal elastic lamina, and injury to medial smooth muscle cells. While restenosis likely results from the interdependent actions of the ensuing inflammation, thrombosis, and smooth muscle cell accumulation (Ferrell, M., et al. (1992) Circ., 85:1630-

1631), the final common pathway evolves as a result of medial VSMC differentiation from a contractile to a secretory phenotype. This involves, principally, VSMC secretion of matrix metalloproteinases degrading the surrounding basement membrane, proliferation and chemotactic migration into the intima, and secretion of a large extracellular matrix, forming the neointimal fibropoliferative lesion. Much of the VSMC phenotypic dedifferentiation after arterial injury mimics that of neoplastic cells (i.e., abnormal proliferation, growth-regulatory molecule and protease secretion, migration and basement invasion). See column 3, lines 30-46. Kinsella discloses that taxol is an antimicrotubule agent that promotes the formation of usually stable microtubules inhibiting the normal dynamic reorganization of the microtubule network required for mitosis and cell proliferation. See column 2, lines 50-60. Kinsella teaches the prevention of recurrent stenosis (restenosis) post therapeutic coronary- or peripheral-artery angioplasty or atherectomy, after coronary bypass graft or stent surgery, or after peripheral vascular surgery (e.g., carotid or other peripheral vessel endarterectomy, vascular bypass, stent or prosthetic graft procedure). A human dosing schedule can consist of (but not be limited to) 24-hour continuous IV pretreatment with up to about 0.5-2 mg/kg (20-80 mg/m.sup.2) prior to the vascular procedure, about 0.25-2 mg/kg (10-80 mg/m.sup.2) continuous IV infusion over the 24 hours post-procedure, then about 0.25-2 mg/kg (10-80 mg/m.sup.2) continuous IV infusion over 24 hours every 21 days for 1 to 6 cycles. Such a dosage is significantly lower than that used to treat human cancers (approximately 4-6 mg/kg). See column 5, lines 40-56. Kinsella teaches the use of 2mg/kg taxol solution reduces the neointima area. See example 5. Kinsella teaches the use of local sustained delivery provide the best solution to prevent restenosis post-angioplasty and

essentially eliminate problems of systemic toxicity. See column 11, lines 10-30. Kinsella teaches administration to cornary and carotid artery.

Westesen et al teach nanoparticles containing various poorly water-soluble drugs. See abstract. Westesen teaches the use of an amorphous form of the drug to provide for better solubility and bioavailability of poorly water-soluble drugs than utilizing a crystalline form. See column 5, lines 45-56. Generally amorphous forms of a substance exhibit a higher solubility and a faster dissolution than the crystals forms since they do not require lattice energy.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to utilize Desai's protein coated drug (antineoplastic drug taxol) for the treatment of proliferation of non-cancerous cells in blood vessels (restenosis). One would have been motivated to do so since Kinsella teaches the use of taxol to reduce atherosclerosis or restenosis since taxol promotes the formation of usually stable microtubules inhibiting the normal dynamic reorganization of the microtubule network required for mitosis and cell proliferation. Furthermore, Desai et al also recognize taxol's unique mode of action on microtubule proteins responsible for the formation of the mitotic spindle. Therefore, one would have expected success by utilizing Desai's taxol to treat abnormal proliferation in the blood vessels since Kinsella teaches taxol is an effective drug that prevents or reduces cell proliferation in the blood vessels.

Conversely, it would have been obvious for one of ordinary skill in the art at the time the invention was made to utilize Desai's protein coated taxol in Kinsella's methodology of treating proliferation of cells in blood vessels. One would have been motivated to do so with the expectation of success since Desai teaches coating taxol with a protein reduces systemic toxicity and may be utilized for targeting specific site in the body and Kinsella teaches the use of taxol in

a local sustained delivery system offer the best solution for treating restenosis and eliminating systemic toxicity.

Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an amorphous drug form. One would have been motivated to do so since Westesen teaches the use of an amorphous form for better solubility and bioavailability of poorly water-soluble drugs. Moreover, one would reasonably expect success by applying Westesen's teachings to Desai since both are directed to poorly water-insoluble drugs.

With regard to claim 75, although Kinsella does not teach administration to the femoral artery specifically, it would have been obvious for a skilled artisan to administer taxol to the artery requiring treatment since Kinsella teaches taxol may be administered to any peripheral artery.

Claims 34, 35, 42, 43, 50-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (5,439, 686) in view of Kinsella et al (5,616,608) in view of Westesen et al (6,197,349) in further view of Hunter (5,994,341).

The teachings of Desai, Kinsella, and Westesen have been discussed above. Desai teaches taxol exhibits a unique mode of action on microtubule proteins responsible for the formation of the mitotic spindle. See column 1, lines 20-30.

The references do not teach the specific use of epothilone as the antiproliferative agent.

Hunter teaches both epothilone and paclitaxel disrupt microtubule function. See column 15, lines 48-55.

It would have been obvious for one of ordinary skill in the art at the time the invention

was made to combine the teaching of the above references and utilize the instantly claimed drug. One would have been motivated to do so with a reasonable expectation of success since Hunter teaches that both paclitaxel and epothilone are both agents which disrupt microtubule function. The selection of a specific drug is considered prima facie obvious to a skilled artisan in the art.

Claims 36-37, 44-45, 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al (5,439, 686) in view of Kinsella et al (5,616,608) in view of Westesen et al (6,197,349) in further view of Gregory (Transplantation, vol. 59, pp. 655-661, 1995).

The teachings of Desai, Kinsella, and Westesen have been discussed above. Desai teaches the use of immunosupressants. See column 5, lines 60-63.

The references do not teach the specific use of rapamycin.

Gregory teaches rapamycin is an immunosuppressant which has an antiproliferative action, that is useful in the treatment of arterial thickening after injury such as angioplasty. See page 655.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to combine the teaching of the above references and further use rapamycin to treat restenosis. One would have been motivated to do so with a reasonable expectation of success since Gregory teaches rapamycin is an immunosuppressant, which has an antiproliferative effect and thus is useful in treating restenosis. Therefore, a skilled artisan would have been motivated to further utilize rapamycin for its additive effect in treating restenosis.

Claims 1, 3, 6-12, 15-17, 31-35, 38-43, 46-51, 54-66, 69-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (5,716,981) by itself or in view of Yapel (4,147,767) in further view of Westesen et al (6,197,349).

Hunter et al teach anti-angiogenic compositions comprising an anti-angiogenic factor and a polymeric carrier and methods of its use. See abstract and column 3, lines 40-45. Preferably the active compound is a compound that disrupts microtubule function such as paclitaxel, epothilone, and etc. see column 3, lines 60-65. The polymeric carrier may be chosen from a carbohydrate, protein, or polypeptide such as albumin, collagen, and gelatin. See column 18, lines 15-30. Hunter teaches using the composition to coat a stent which is inserted into the body. Delivery may be done through via expandable catheters. See column 4, lines 24-30 and column 22. Hunter teaches the use of the composition to treat non-tumorigenic angiogenesis dependent diseases. See column 5, lines 44-46 and column 36, lines 9-15. Specifically Hunter teaches methods of eliminating vascular obstructions in arteries and veins to prevent recurrent stenosis at the site of failed angioplasty and to treat post surgical narrowing. Suitable sites of the stent include iliac, renal, and femoral, and cornary arteries. See column 25, lines 48-67. Hunter teaches treating neointimal hyperplasia wherein a stent is coated with the composition and inserted onto the arteries. See column 36, lines 1-20. The composition may be further administered intarticularly, intravenously, etc. see column 37, line 67 to column 38, lines 1-10. The microspheres range from 50-nm to 500 microns depending on the particular use. See column 17, lines 25-40. Anti-angiogenic factors may be linked by occlusion in the matrices of the polymer, bound by covalent linkages, or encapsulated in microcapsules. See column 17, lines 1-5.

The use of albumin as the polymeric carrier is not immediately envisaged.

Yapel teaches albumin (HAS) medicament carrier suited fro intravascular injections. Yapel teaches compared to prior art polymeric carriers has advantages such as ability to administer insoluble drugs; localizes the drug in the capillaries and the drug is released at the intended sire and reduces toxic side effects which is especially useful for anti-neoplastic drugs; the absence of emboli formation wherein albumin carriers are administered; ease of preparation; nonantigenicity; capability of carrying a variety of drugs. See column 2, line 50 to column 3, lines 30.

Westesen et al teach nanoparticles containing various poorly water-soluble drugs. See abstract. Westesen teaches the use of an amorphous form of the drug to provide for better solubility and bioavailability of poorly water-soluble drugs than utilizing a crystalline form. See column 5, lines 45-56. Generally amorphous forms of a substance exhibit a higher solubility and a faster dissolution than the crystals forms since they do not require lattice energy.

Firstly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Hunter and utilize albumin as the polymer of choice. One would have been motivated to do so with a reasonable expectation of success and similar results since Hunter suggests proteins and polypeptides such as albumin are suitable as the polymeric carrier.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hunter and Yapel and specifically utilize albumin as the polymeric carrier. One would have been motivated to do so since Yapel teaches

the advantages of using albumin as the polymeric carrier including nonantigenicity, localized and targeted delivery which reduces toxicity of anti-neoplastic drugs, ease of preparation, etc.

Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an amorphous drug form. One would have been motivated to do so since Westesen teaches the use of an amorphous form for better solubility and bioavailability of poorly water-soluble drugs.

Claims 4-5, 13-14, 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (5,716,981) by itself or in view of Yapel (4,147,767) in view of Westesen et al (6,197,349) in further view of Kinsella et al (5,616,608).

The disclosure of Hunter, Yapel, and Westesen have been set forth above.

The references do not specify the dosage amount and dosing cycle.

Kinsella teaches a method of treating atherosclerosis or restenosis using microtubule stabilizing agent such as taxol or taxol derivatives. During angioplasty, intraarterial balloon catheter inflation results in endothelialization, disruption of the internal elastic lamina, and injury to medial smooth muscle cells. Kinsella discloses that taxol is an antimicrotubule agent that promotes the formation of usually stable microtubules inhibiting the normal dynamic reorganization of the microtubule network required for mitosis and cell proliferation. See column 2, lines 50-60. Kinsella teaches the prevention of recurrent stenosis (restenosis) post therapeutic coronary- or peripheral-artery angioplasty or atherectomy, after coronary bypass graft or stent surgery, or after peripheral vascular surgery (e.g., carotid or other peripheral vessel endarterectomy, vascular bypass, stent or prosthetic graft procedure). A human dosing schedule can consist of (but not be limited to) 24-hour continuous IV pretreatment with up to about 0.5-2

mg/kg (20-80 mg/m.sup.2) prior to the vascular procedure, about 0.25-2 mg/kg (10-80 mg/m.sup.2) continuous IV infusion over the 24 hours post-procedure, then about 0.25-2 mg/kg (10-80 mg/m.sup.2) continuous IV infusion over 24 hours every 21 days for 1 to 6 cycles. Such a dosage is significantly lower than that used to treat human cancers (approximately 4-6 mg/kg). See column 5, lines 40-56. Kinsella teaches the use of 2mg/kg taxol solution reduces the neointima area. See example 5. Kinsella teaches the use of local sustained delivery provide the best solution to prevent restenosis post-angioplasty and essentially eliminate problems of systemic toxicity. See column 11, lines 10-30. Kinsella teaches administration to cornary and carotid artery.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the above references and further look to Kinsella for the dosage amount of taxol and the dosing cycle. One would have been motivated to do so with a reasonable expectation of success and similar results since both Hunter and Kinsella teach the treatment of recurrent stenosis and neointimal hyperplasia with drugs that inhibit microtubule function such as taxol.

Claims 36-37, 44-45, 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (5,716,981) by itself or in view of Yapel (4,147,767) in view of Westesen et al (6,197,349) in further in view of Marx (Circ. Res. Vol. 76, pp. 412-417, 1995).

The disclosure of Hunter, Yapel, and Westesen have been set forth above.

The references do not teach the specific use of rapamycin as the antiproliferative agent.

Marx teaches rapamycin is an inhibitor of smooth muscle cells in the abnormal proliferation of restenosis. See abstract.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to combine the teaching of the above references and utilize the instantly claimed drugs. One would have been motivated to do so with a reasonable expectation of success since Marx teaches the rapamycin is a smooth cell inhibitor useful in treating restenosis. The selection of a specific drug is considered prima facie obvious to a skilled artisan in the art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-41, 46-49, 52-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 11-20, 44-48 of copending Application No. 11/544242; instant claims 1, 3-17, 31-32, 38-40, 46-48, 54-78 over

claims 1, 5-13, 16-17, 21, 24 of 11/594417; and instant claims1, 5-13, 16-17, 21, 24 over claims 1-2, 5-18, 11/359286 respectively in view of Kinsella et al (5,616,608).

The instant application is directed to a method of treating hyperplasia in the blood vessels and a method of reducing proliferation in vascular procedures comprising administering a antineoplastic; antiproliferative; or angiogenesis inhibitor coated with a protein.

Copending application '286 is directed to a method of treating a proliferative disease in an individual comprising administering to the individual: a) an effective amount of a composition comprising nanoparticles comprising a taxane and an albumin, and b) an effective amount of at least one other chemotherapeutic agent, wherein said chemotherapeutic agent is selected from the group consisting of antimetabolites, platinum-based agents, alkylating agents, tyrosine kinase inhibitors, anthracycline antibiotics, vinca alkloids, proteasome inhibitors, macrolides, and topoisomerase inhibitors. Dependent claims are directed to rapamycin, albumin, the instant route of administration; and particle size.

Copending application '242 is directed a method of treating a proliferative disease in an individual, comprising administering to the individual an effective amount of a composition comprising nanoparticles comprising a thiocolchicine (antineoplastic) or a derivative thereof and a carrier protein. Independent claim 13 is directed to treating a proliferative diseases comprising administering nanoparticles comprising orataxel and protein. Dependent claims are directed to albumin, the instant route of administration; and particle size.

Copending application '286 is directed to a method of treating a proliferative disease in an individual, comprising administering to the individual an effective amount of a composition

comprising nanoparticles comprising a taxane and a carrier protein. Dependent claims are directed to albumin, the instant route of administration; and particle size.

The copending applications do not specify the proliferative disease.

Kinsella teaches a method of treating atherosclerosis or restenosis using microtubule stabilizing agent such as taxol or taxol derivatives. It should be noted that restenosis is the excessive proliferation of smooth muscle cells, i.e. non-cancerous cells, in the blood vessel. During angioplasty, intraarterial balloon catheter inflation results in endothelialization, disruption of the internal elastic lamina, and injury to medial smooth muscle cells. While restenosis likely results from the interdependent actions of the ensuing inflammation, thrombosis, and smooth muscle cell accumulation (Ferrell, M., et al. (1992) Circ., 85:1630-1631), the final common pathway evolves as a result of medial VSMC differentiation from a contractile to a secretory phenotype. This involves, principally, VSMC secretion of matrix metalloproteinases degrading the surrounding basement membrane, proliferation and chemotactic migration into the intima, and secretion of a large extracellular matrix, forming the neointimal fibropoliferative lesion. Much of the VSMC phenotypic dedifferentiation after arterial injury mimics that of neoplastic cells (i.e., abnormal proliferation, growth-regulatory molecule and protease secretion, migration and basement invasion). See column 3, lines 30-46. Kinsella discloses that taxol is an antimicrotubule agent that promotes the formation of usually stable microtubules inhibiting the normal dynamic reorganization of the microtubule network required for mitosis and cell proliferation. See column 2, lines 50-60. Kinsella teaches the prevention of recurrent stenosis (restenosis) post therapeutic coronary- or peripheral-artery angioplasty or atherectomy, after coronary bypass graft or stent surgery, or after peripheral vascular surgery

(e.g., carotid or other peripheral vessel endarterectomy, vascular bypass, stent or prosthetic graft procedure). A human dosing schedule can consist of (but not be limited to) 24-hour continuous IV pretreatment with up to about 0.5-2 mg/kg (20-80 mg/m.sup.2) prior to the vascular procedure, about 0.25-2 mg/kg (10-80 mg/m.sup.2) continuous IV infusion over the 24 hours post-procedure, then about 0.25-2 mg/kg (10-80 mg/m.sup.2) continuous IV infusion over 24 hours every 21 days for 1 to 6 cycles. Such a dosage is significantly lower than that used to treat human cancers (approximately 4-6 mg/kg). See column 5, lines 40-56. Kinsella teaches the use of 2mg/kg taxol solution reduces the neointima area. See example 5. Kinsella teaches the use of local sustained delivery provide the best solution to prevent restenosis post-angioplasty and essentially eliminate problems of systemic toxicity. See column 11, lines 10-30. Kinsella teaches administration to cornary and carotid artery.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the copending applications and Kinsella to arrive at the instantly claimed invention of treating hyperplasia of blood vessels. One would have been motivated to do so since Kinsella teaches neointimal hyperplasia is a proliferative disease that can be treated with anti-neoplastic drugs that disrupt microtubule function. Therefore, although the copending application do not specify treating hyperplasia, instant application and copending applications are directed to similar subject matter since hyperplasia is a proliferative disease.

This is a provisional obviousness-type double patenting rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila S. Gollamudi
Primary Examiner
Art Unit 1616